REMARKS

Applicants respectfully request entry of the Amendment and reconsideration of the claims.

Claims 1-26 and 30-31 have been canceled without prejudice or disclaimer. Claims 1-26 and 30-31 were withdrawn due to a restriction requirement. Applicants reserve the right to pursue the subject matter of these claims in one or more continuation applications.

Claims 32-39 are newly presented. Applicants submit the new claims are supported throughout the specification, including at lines 7-16 on page 1, lines 8-17 on page 4, lines 17-30 on page 49, Figures 3A and 3B, lines 9-17 on page 50, line 26 on page 50 to line 7 on page 51, Figures 4A, 4B and 4C, and Example 7 on page 54, and do not raise any issues of new matter.

Claims 27-29 have been amended. Applicants submit the amendments are supported throughout the specification, including at page 6, lines 14-24; page 20, lines 2-18; and page 50, line 1 to page 51, line 7.

Specification

The Examiner objected to the specification for not complying with the sequence rules. The Examiner indicated that Applicants should amend Figure 2 or the brief description of the drawings to include sequence identifiers for the amino acid sequences shown the figure. Applicants amended the brief description of the drawings to include a sequence identifier for each amino acid sequence shown in Figure 2. Withdrawal of the objection is respectfully requested.

Claim Objection

Claims 27-29 were objected to because of informalities in the claims. Applicants defined the abbreviation "BFIT" as required by the Examiner. Withdrawal of the objection is respectfully requested.

Indefinite

Claims 27-29 were rejected under 35 U.S.C. § 112, second paragraph, as indefinite. Applicants submit the claims as amended obviate the rejection of the claims under 35 U.S.C. § 112, second paragraph. Withdrawal of the rejection is respectfully requested.

Utility

Claims 27-29 were rejected under 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph, as lacking utility. The Examiner contends that screening for any metabolic disease is not specific and substantial. Applicants respectfully traverse.

The Examiner maintains the asserted utility of the method for screening for a metabolic disease is not substantial or specific. Applicants submit that the Examiner has not established a prima facie case of lack of utility. Applicants submit that one of skill in the art would find Applicants' asserted utility to more likely than not to be true. Applicants submit that absolute certainty is not required.

Applicants submit that the Examiner is requiring Applicants to establish utility to a higher degree of certainty than is required. Applicants do not have to provide evidence sufficient to establish that an asserted utility is true beyond a reasonable doubt. *In re Irons*, 340 F.2d 974, 978 (CCPA 1965). Nor do Applicants have to provide evidence that establishes the asserted utility as a matter of statistical certainty. *Nelson v. Bowler*, 626 F.2d 853, 856-867 (CCPA 1980). Rather, Applicants only have the burden of presenting evidence that leads a person of ordinary skill in the art to conclude that the asserted utility is more likely than not true. MPEP § 2107.02 (emphasis in original). Applicants submit that the evidence that they have provided establishes that the utility asserted is more likely than not to be true.

Applicants' claims as amended are directed to method of screening for a predisposition to obesity by measuring expression of a polynucleotide encoding a brown fat inducible thioesterase comprising at least 92% sequence identity to SEQ ID NO:2, SEQ ID NO:4 or SEQ ID NO:6, wherein the polypeptide has thioesterase activity, in a tissue sample of a patient, and comparing the expression of the polynucleotide to a control sample, wherein decreased expression of the polynucleotide as compared to the control sample indicates a predisposition to obesity.

The Examiner asserts that obese prone mice fed a high fat diet showed increased expression of BFIT and that there is no indication that obese prone mice showed an increase gene expression of BFIT as opposed to obese resistant mice in the absence of a high fat diet. Applicants disagree with this characterization of the data presented in the specification.

Applicants direct the Examiner's attention to pages 49-51 and Figure 3. The data prescribed in the specification shows that BFIT is strongly induced in the brown adipose tissue of mice exposed to cold, and shows decreased expression in brown adipose tissue from mice in a thermal neutral environment. At page 50, line 23, to page 51, line 8, and Figure 4. The Applicants describe that BFIT was elevated in brown adipose tissue of obesity resistant SWR/J mice as compared to obesity prone AKR/J mice. (Figure 4). Obesity resistant mice fed a high fat diet revealed a 2-fold higher expression of BFIT as compared to obesity prone mice, C57B116J. (Figure 4B). Finally, the specification indicates BFIT in nonobese mice Ob/? was 2.5 fold higher compared to obese mice (ob/ob, Figure 4C). Moreover, the Applicants also indicate that BFIT expression in food-restricted mice was enhanced to the same levels in cold challenged mice. (See the specification at page 52, lines 12-23.) In several models, the data shows that BFIT expression is lower in obese mice. Applicants submit that this data supports the asserted utility of screening a patient for a predisposition for obesity by detecting a decrease in expression of a polynucleotide encoding a BFIT polypeptide comprising 92% sequence identity to SEQ ID NO:2, SEQ ID NO:4, or SEQ ID NO:6, wherein the polypeptide has thioesterase activity.

Applicants submit that one of skill in the art reading the specification would conclude that Applicants asserted utility was more likely than not true. Applicants have shown in several models that expression of a BFIT polypeptide is decreased in obese mice. Thus, Applicants respectfully request withdrawal of the 35 U.S.C. § 101 rejection.

The Examiner also rejected claims 27-29 under 35 U.S.C. § 112, first paragraph, for lacking enablement. The Examiner contends that the specification does not enable any utility. Applicants respectfully traverse.

In order to make a rejection, the Examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. *In re Wright*, 999 F.2d 1557, 1562 (Fed. Cir. 1993); MPEP §2164.04. "[I]t is incumbent upon the Patent Office,

whenever a rejection on this basis [enablement] is made, to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement." *In re Marzocchi*, 439 F.2d 220, 224 (CCPA 1971); MPEP §2164.04. Further, a patent need not teach, and preferably omits, what is well known in the art. *In re Buchner*, 929 F.2d 660, 661 (Fed. Cir. 1991); MPEP §2164.01.

Applicants respectfully submit that the specification provides enablement for the claims. As discussed previously, Applicants have described several utilities. Those utilities include methods of screening for metabolic disease and methods for monitoring metabolism. See the specification at page 5, line 5 to page 6, line 23. Moreover, Applicants have provided several working examples showing upregulation of BFIT expression in cells from obese resistant or non-obese mice as compared to obese mice. See the specification at page 44 to page 54. The results show the expression of BFIT as enhanced in cells of non-obese or obese resistant mice as compared to obese mice. Applicants submit that these description in the specification and the working examples provide for enablement of the claims. Applicants respectfully request withdrawal of the rejection.

Written Description

Claims 27-29 were rejected under 35 U.S.C. § 112, first paragraph, as lacking written description.

Applicants remind the Examiner that the written description requirement requires that Applicants' specification must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, that he or she was in possession of the invention. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). A written description of an invention involving a chemical genus requires a precise definition, such as by structure, formula ... of the claimed subject matter sufficient to distinguish it from other materials. Univ. of California v. Eli Lilly and Co., 43 USPQ2d 1398. 1405 (Fed. Cir. 1997) (emphasis added). Since one skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass, such a formula is normally an adequate description of the claimed invention. Id. at 1406 (emphasis added). Moreover, as noted in the Guidelines for Examination of Patent

Applications Under 35 U.S.C. § 112, ¶1, "Written Description" Requirement ("the guidelines"), there is a "strong presumption" that an adequate written description of the claimed invention is present when the application is filed, 66(4) Fed Reg. 1099, 1105 (2001); see also, In re Wertheim, 191 USPQ 90,97 (CCPA 1976). The guidelines further state that "[(The examiner has the initial burden of presenting by a preponderance of evidence why a person skilled in the art would not recognize in an Applicants' disclosure a description of the invention defined by the claims." 66(4) Fed. Reg. at 1107; 191 USPQ at 97, (emphasis added).

Compliance with the written description requirement does not require an applicant to describe exactly the subject matter claimed; rather, the description must clearly allow a person of ordinary skill in the art to recognize that he or she invented what is claimed. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). The test is whether the originally filed specification reasonably conveys to a person having ordinary skill in the art that applicant had possession of the subject matter later claimed. In re Kaslow, 217 USPQ 1089 (Fed. Cir. 1991). Moreover, in order to have possession of members of a claimed genus, the specification need not describe all of the species that the genus encompasses. Amgen Inc. v. Chugai Pharmaceutical Co., 18 USPQ2d 1016, 1027 (Fed. Cir. 1991).

The Examiner contends that the specification has not provided written description for a method of screening a patient for a genus of metabolic diseases. Applicants disagree. At page 5, lines 10-15 of the specification, Applicants have described that metabolic diseases include obesity, wasting disease such as cachexia and diabetes. Applicants also further describe using BFIT polypeptides and polynucleotides in clinical screens to test for metabolic disease etiology or to assess the level of risk for these disorders. (See the specification at page 6, line 14 to line 23.) In addition, Applicants have described and provided working examples of detecting BFIT mRNA in a variety of tissues. See the specification at page 51, line 10 to page 52, line 7, and Figure 6. Thus, Applicants respectfully request withdrawal of the rejection on this basis.

The Examiner also rejected the claims for lacking written description because the Examiner contends that the polypeptides required to practice the claimed method are members of a large structurally variable genus. Applicants respectfully traverse.

As discussed above, Applicants submit that providing the polypeptide and polynucleotide sequences allows one of skill in the art to identify members of the genus. Applicants submit they

have adequately described the genus of polynucleotides and/or polypeptides as claimed in the methods. Applicants have described three different polypeptides (SEQ ID NO:2, SEQ ID NO:4, and SEQ ID NO:6). Applicants have provided an alignment of the three sequences in Figure 2. Applicants have also described the polynucleotide encodes a polypeptide that has 92% sequence identity to SEQ ID NO:2, SEQ ID NO:4, or SEQ ID NO:6 and that has thioesterase activity. Applicants note that the human BFIT1 and human BFIT2 have 92% sequence identity. Applicants have also described various domains of these proteins. In Figure 2, bars denote the G-X-H motifs conserved in thioesterase proteins. The start lipid binding domains and the two acyl-COA thioesterase domains are also described. See page 49, lines 8-16.

Thus, Applicants submit that the specification does provide written description for the methods as claimed because both the structure and function of the compounds useful in the method are described. Applicants respectfully request withdrawal of the rejection on this basis

Enablement

Claims 27-29 were rejected under 35 U.S.C. § 112, first paragraph as lacking enablement. The Examiner contends claims 27-29 lack an enablement. The Examiner contends the specification does enable a method for screening a patient for obesity predisposition by measuring expression of a polynucleotide encoding a polypeptide of SEQ ID NO:2, SEQ ID NO:4, or SEQ ID NO:6. Applicants submit that the claims as amended are similar to that which the Examiner indicated were enabled by the specification.

Moreover, Applicants submit that they have enabled a method using a polynucleotide encoding a BFIT polypeptide that comprise 92% sequence identity to SEQ ID NO:2, SEQ ID NO:4, or SEQ ID NO:6, and wherein the BFIT polypeptide has thioesterase activity. Applicants submit that human BFIT1 and human BFIT2 have about 92% sequence identity. Applicants have provided working examples for detecting expression of both of these polynucleotides encoding these polypeptides at page 45, line 22, to page 46, line 16. Tissue specificity of expression of both hBFIT1 and hBFIT2 was performed as described at page 51, line 10, to page 52, line 7. In addition, as discussed previously, Applicants have shown in several models a decreased expression of a polynucleotide encoding BFIT is associated with obesity.

Thus, Applicants submit they have enabled the claimed invention and respectfully request withdrawal of the rejection on this basis.

Conclusion

In view of the Amendment and Remarks, Applicants respectfully request a Notice of Allowance. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Respectfully submitted,

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